National Clinical Trials Network Groups
Update Fall 2014

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NRG ONCOLOGY™

NCTN Groups Update

- **Why Continue the Groups?**
- **NCTN Groups vs Cooperative Groups: Any Real Difference?**
- **NCTN Current Trials: A Few Examples**
- **NCTN Structure and Governance Challenges**

Why Continue the Groups?

- Practice-Defining, Paradigm-Shifting Research
- Cost Effective ($150-160 M/yr NCI Funding for 12 yrs)
  - 90+% Volunteer Physician Effort
  - Cost Effectiveness Confirmed in NCI-Supported Review
  - A System Impossible to Replicate at Current Cost
- Alignment with all major US & Canadian Cancer Centers
- Many Group Trials not Feasible at Centers or with Pharma

Why Change the Groups?

- Institute of Medicine Recommendations 2010
  - More Efficient System with Shorter Timelines
  - Align Groups with New Science More Effectively
  - Restore Groups' Funding to Recommended Levels
  - Reduce Oversight of NCI over Group Research
  - More Trials for Pts with Rare Malignancies

Is NCTN Meaningfully Different than Old System?

- Fewer Groups: Coordination of Groups Easier
  Reduced Career Opportunities
- Better Coordination: Too Early to Tell
  Need Governance Structure
- More Cost Effective? Unclear
  $ Distribution is Different
- More Timely/Efficient: Efficiency Efforts in Place
- Rare Disease Trials: No
- Alignment with Science: Already Happening

Current NCTN Lung Cancer Trial Examples

- **Precision Medicine Effort in Cancer Trials**
  - **Lung MAP:** **SWOG 1400**
  - **ALCHEMIST:** **Alliance/ECOG ACRIN**
  - **Stage III Lung Cancer** **NRG 1306/Alliance 31101**

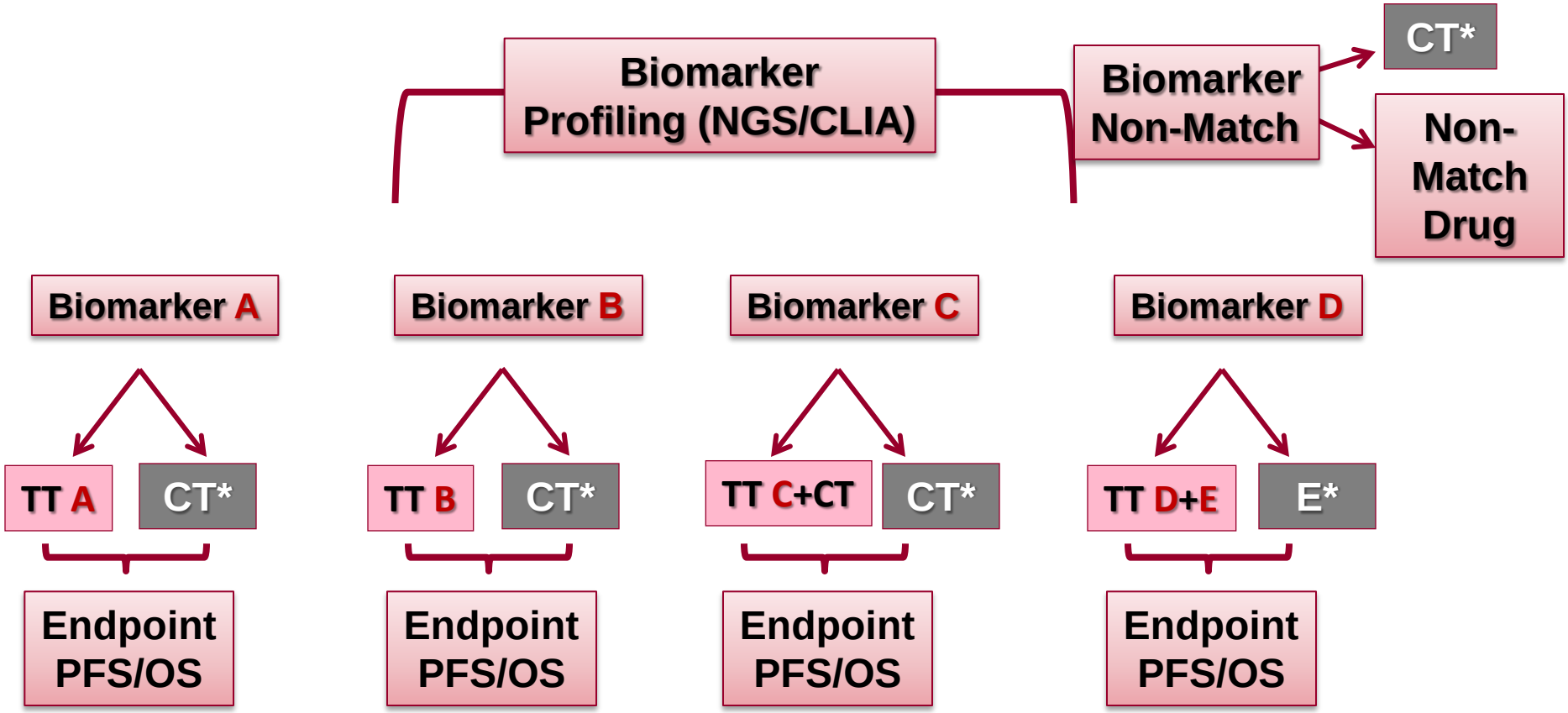
- **Innovative Rad Oncology Trials for Stage III NSCLC Pts**
  - **Adaptive Radiotherapy** **NRG/RTOG 1106**
  - **Proton Beam vs IMRT** **NRG/RTOG 1308**

None of These Trials are Doable in Any Other System

LUNG-MAP (S1400): A Biomarker-driven Multi-Arm Master Phase II/III Trial in Squamous Lung Cancer 2nd line Therapy

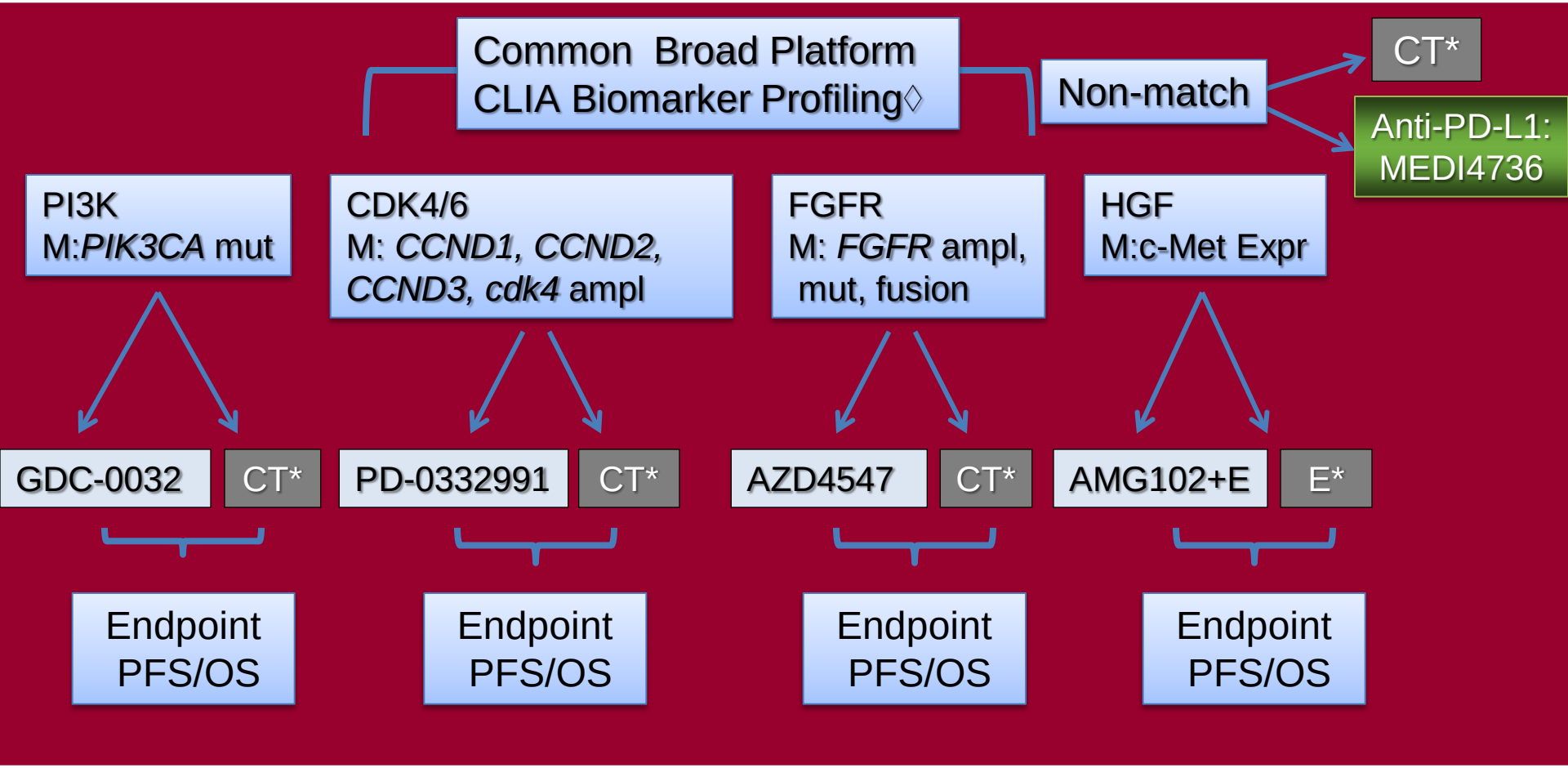
LUNG-MAP

S1400: LUNG-MAP: Squamous Lung Cancer- 2nd Line Therapy



S1400

LUNG-MAP



TT=Targeted therapy, CT=chemotherapy (docetaxel or gemcitabine), E=erlotinib

◊ Archival FFPE tumor, fresh CNB if needed

ALCHEMIST

(Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials)

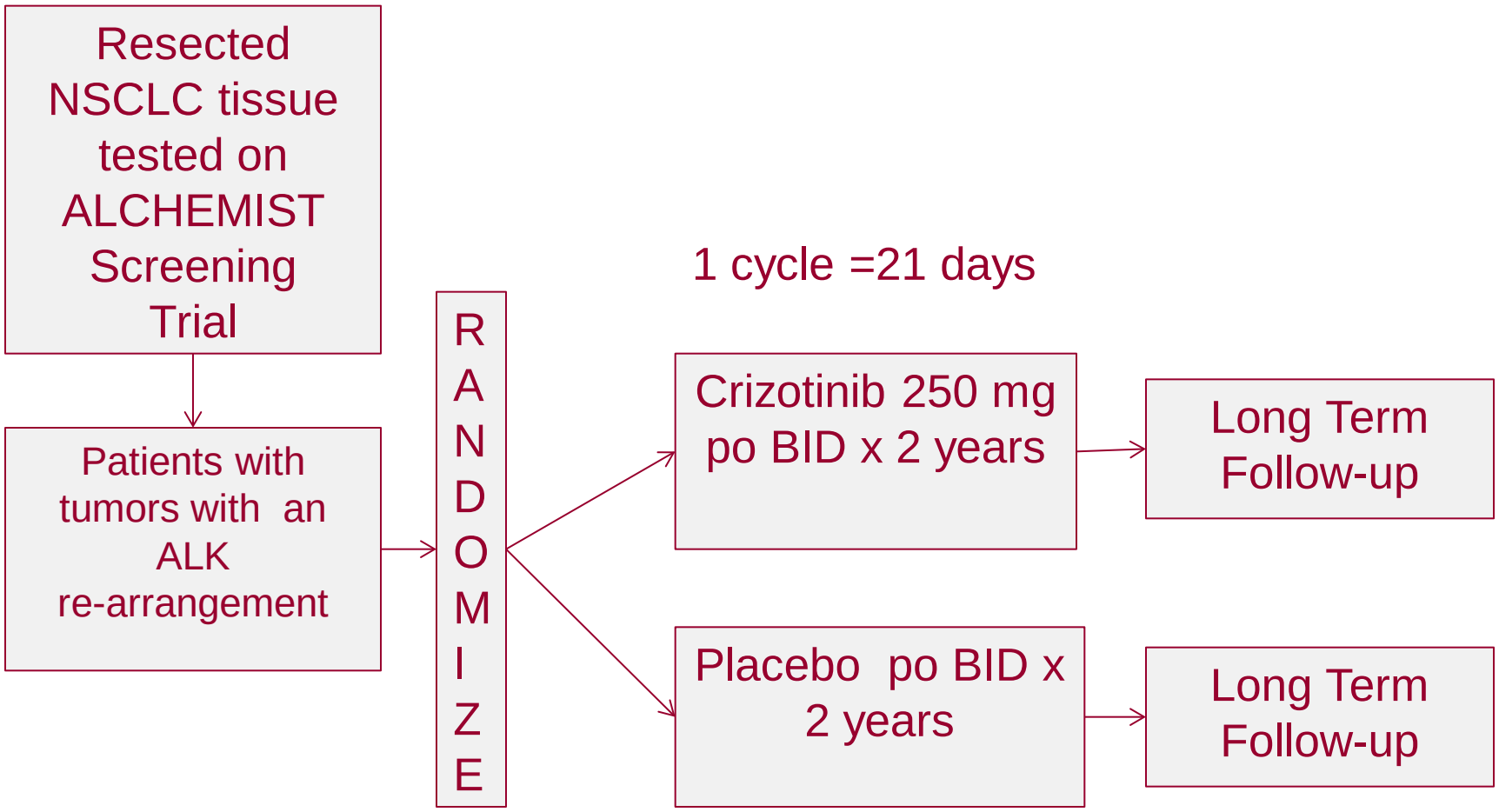
3 Integrated Trials Testing Targeted Therapy

in Early Stage Lung Cancer

ALCHEMIST Rationale

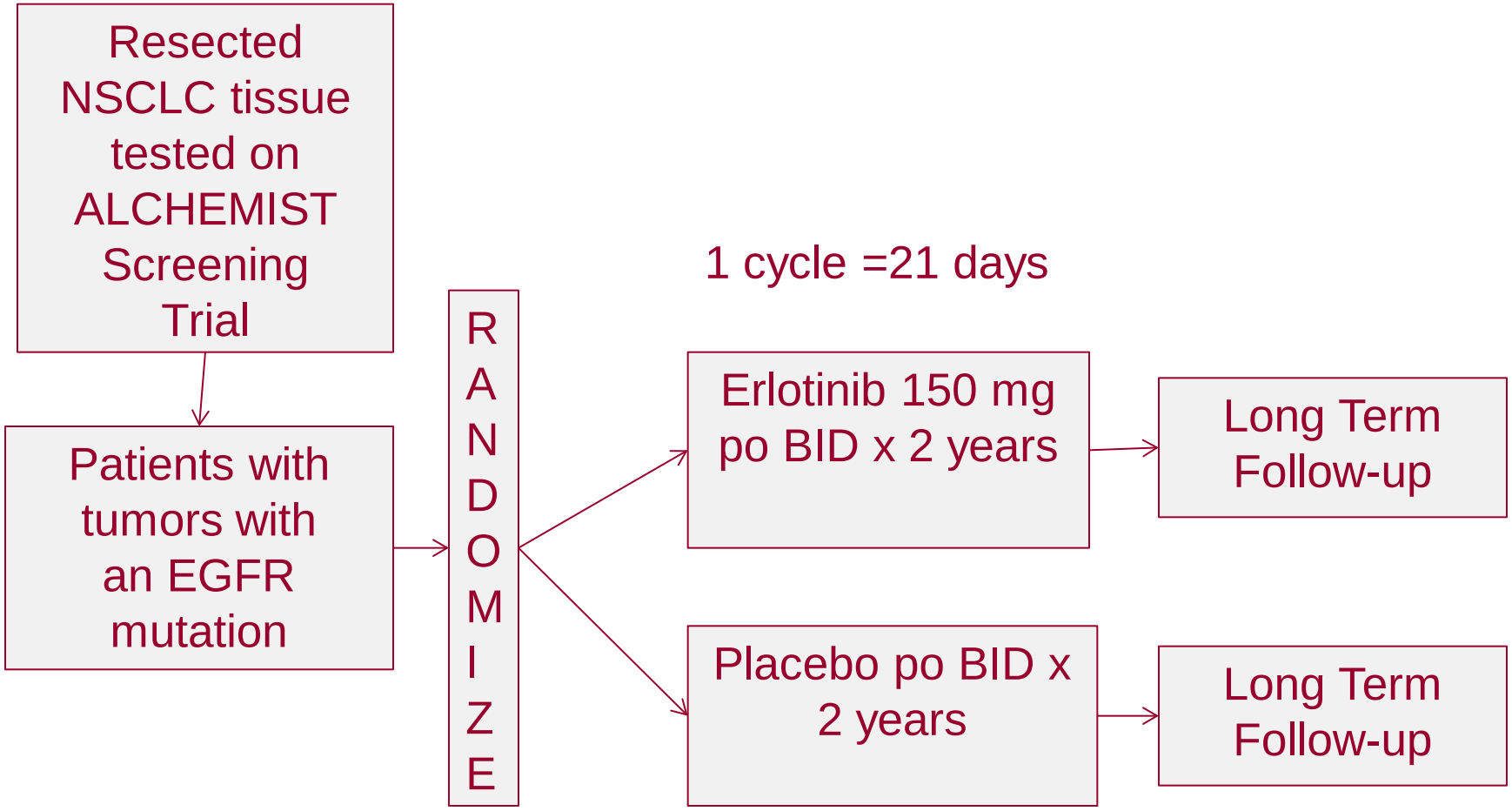
- ALCHEMIST is studying whether or not treatment based on genotype improves cure rates in earlier stage (IB-IIIA) NSCLC cancer patients with non-squamous tumors that have been completely surgically resected.

ALCHEMIST ALK Treatment Trial E4512



Primary endpoint is overall survival

ALCHEMIST EGFR Treatment Trial A081105



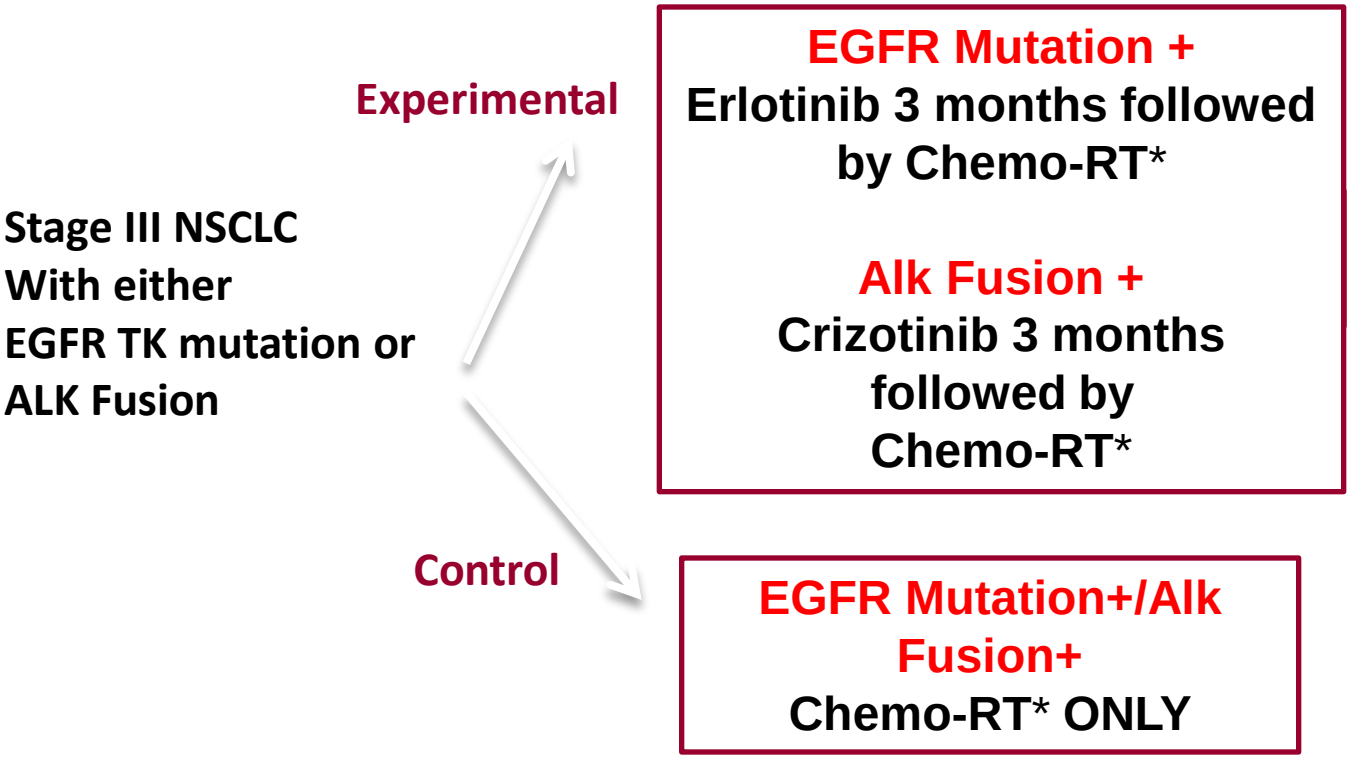
Primary endpoint is overall survival

NRG/RTOG 1306/Alliance 31101

A RANDOMIZED PHASE II STUDY OF INDIVIDUALIZED COMBINED MODALITY THERAPY FOR STAGE III NON-SMALL CELL LUNG CANCER (NSCLC)

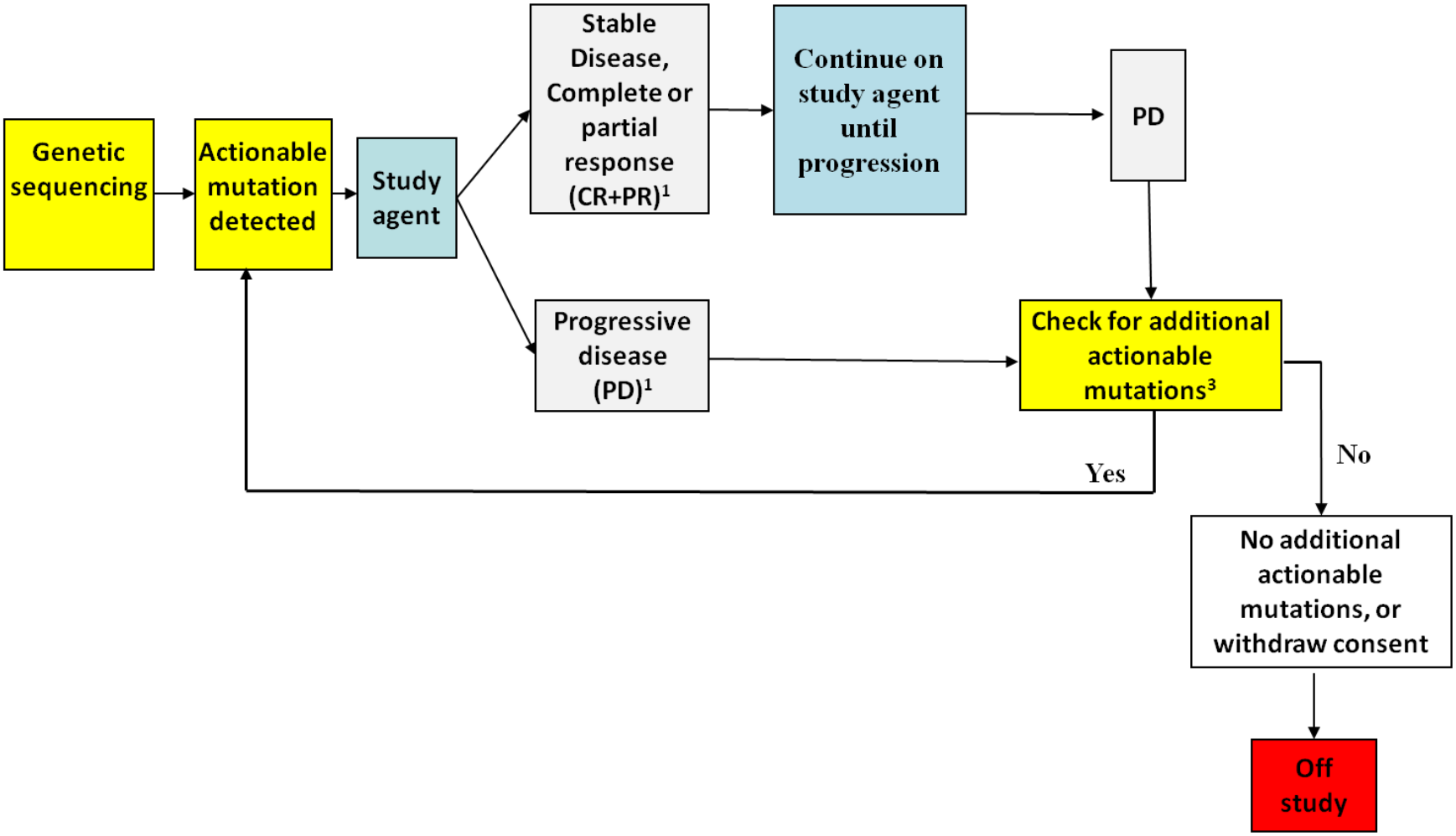
NRG/RTOG 1306/ Alliance 31101

A Randomized Phase II Trial

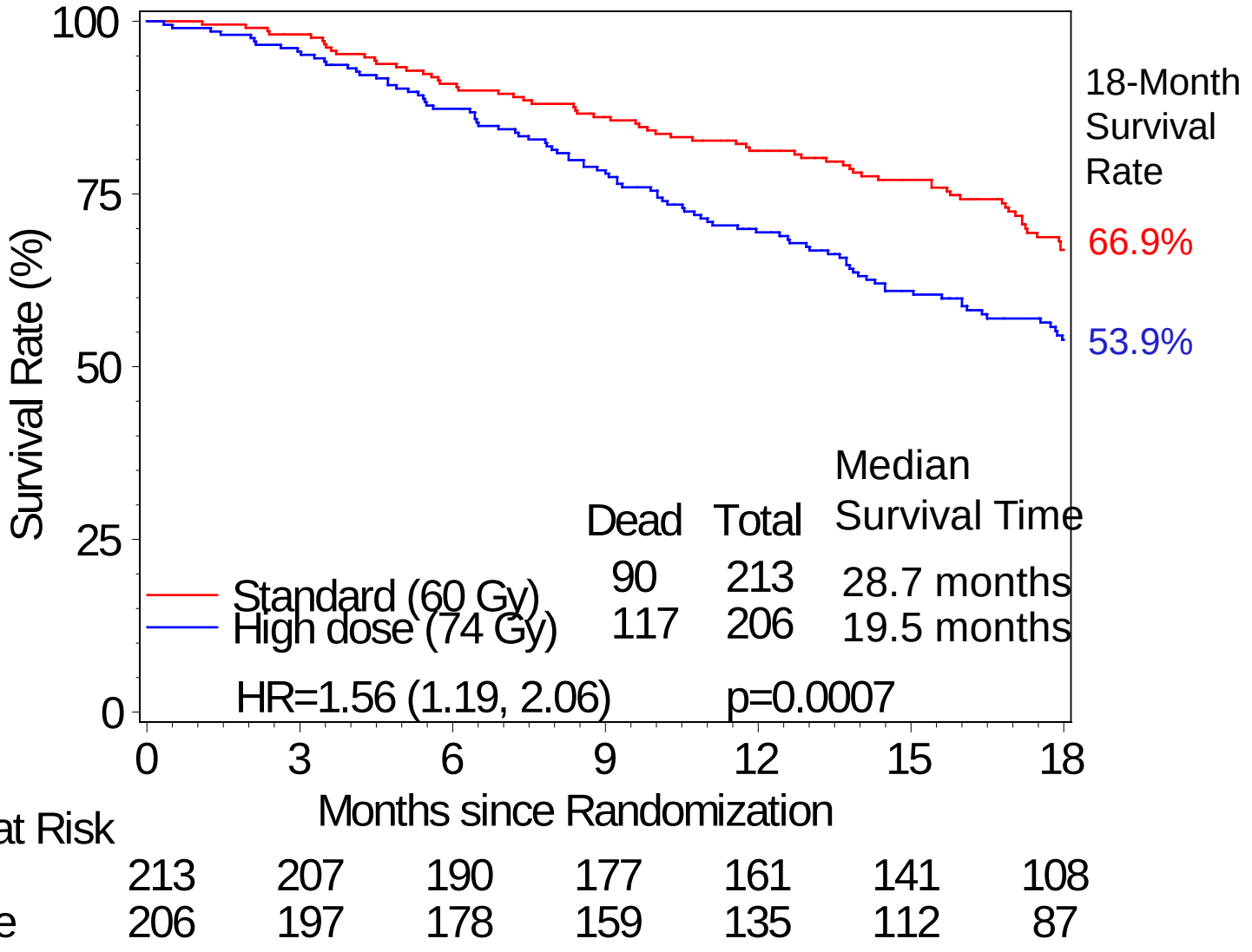


*Pemetrexed 500 mg/m^2 q 3 weekly x 4 Carboplatin AUC 5 (4 cycles) with Thoracic Radiation 60 Gy

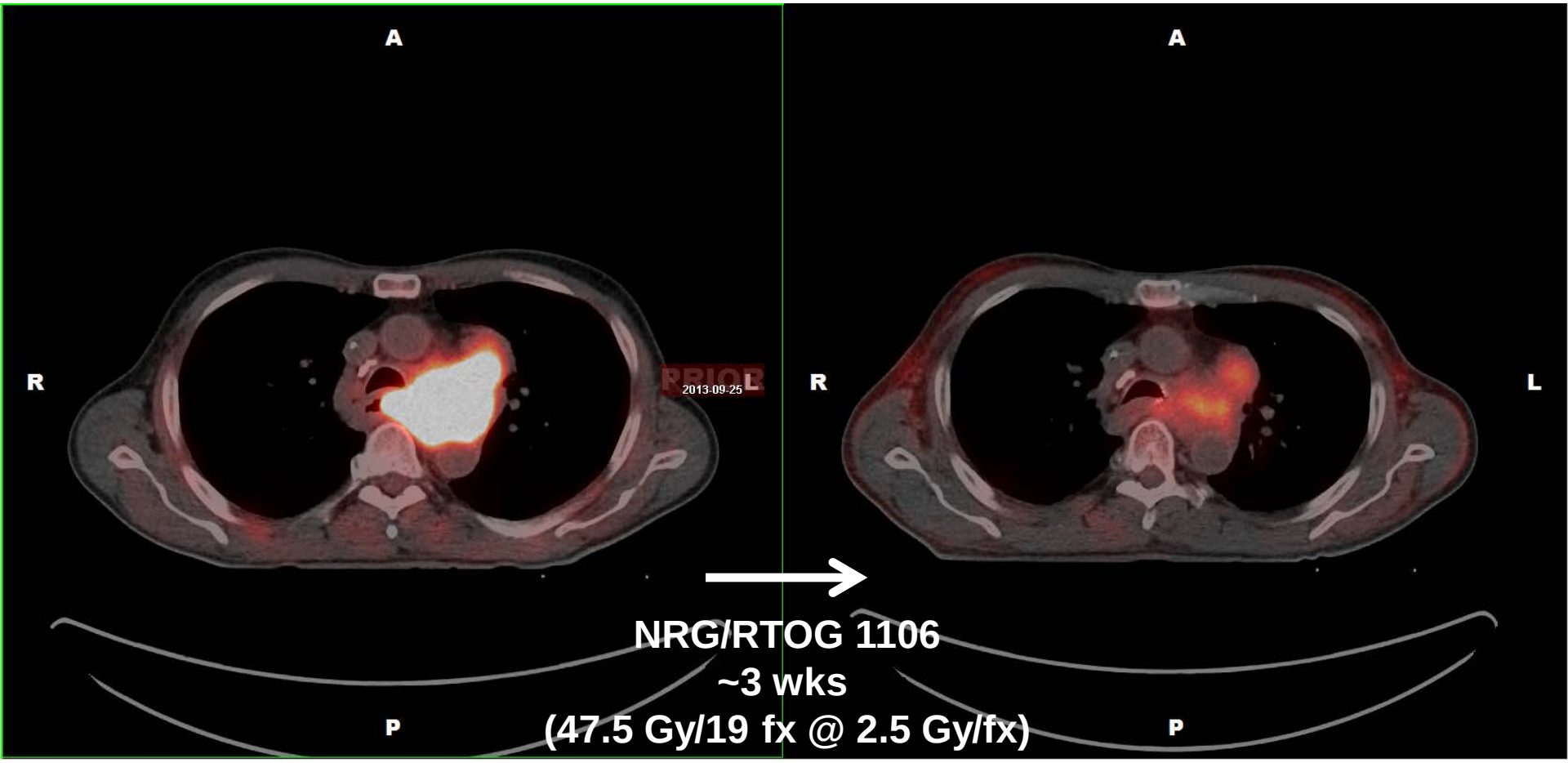
MATCH TRIAL DESIGN



NRG/RTOG 0617: Survival by RT Dose

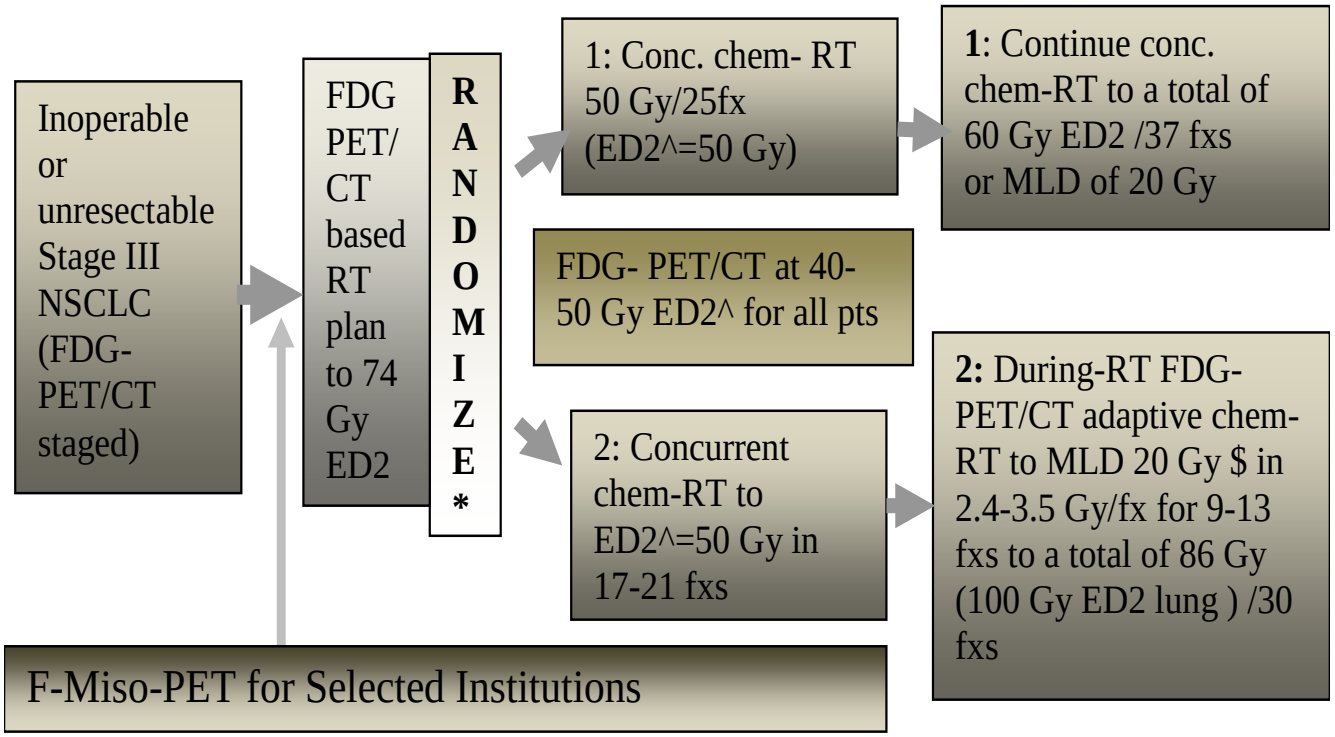


PET-Adapted Radiation Therapy



NRG/RTOG 1106-Adaptive RT for Stage III NSCLC Pts

NRG/RTOG 1106 tests the efficacy of during-RT PET-MTV based individualized radiation dose escalation.

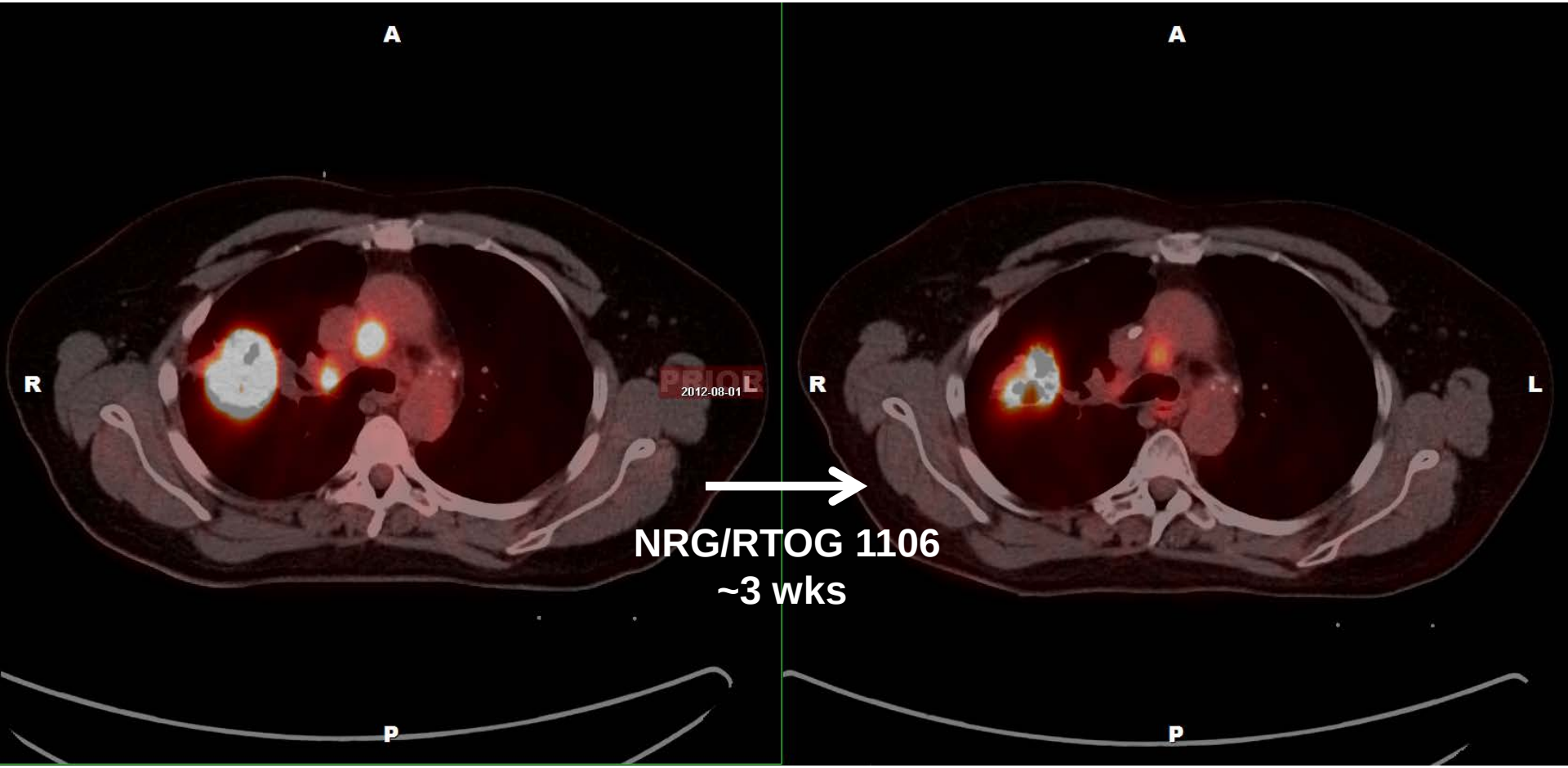


RTOG 0617
Uniform RT dose prescription

Individualized adaptive RT

PET-Adapted Radiation Therapy

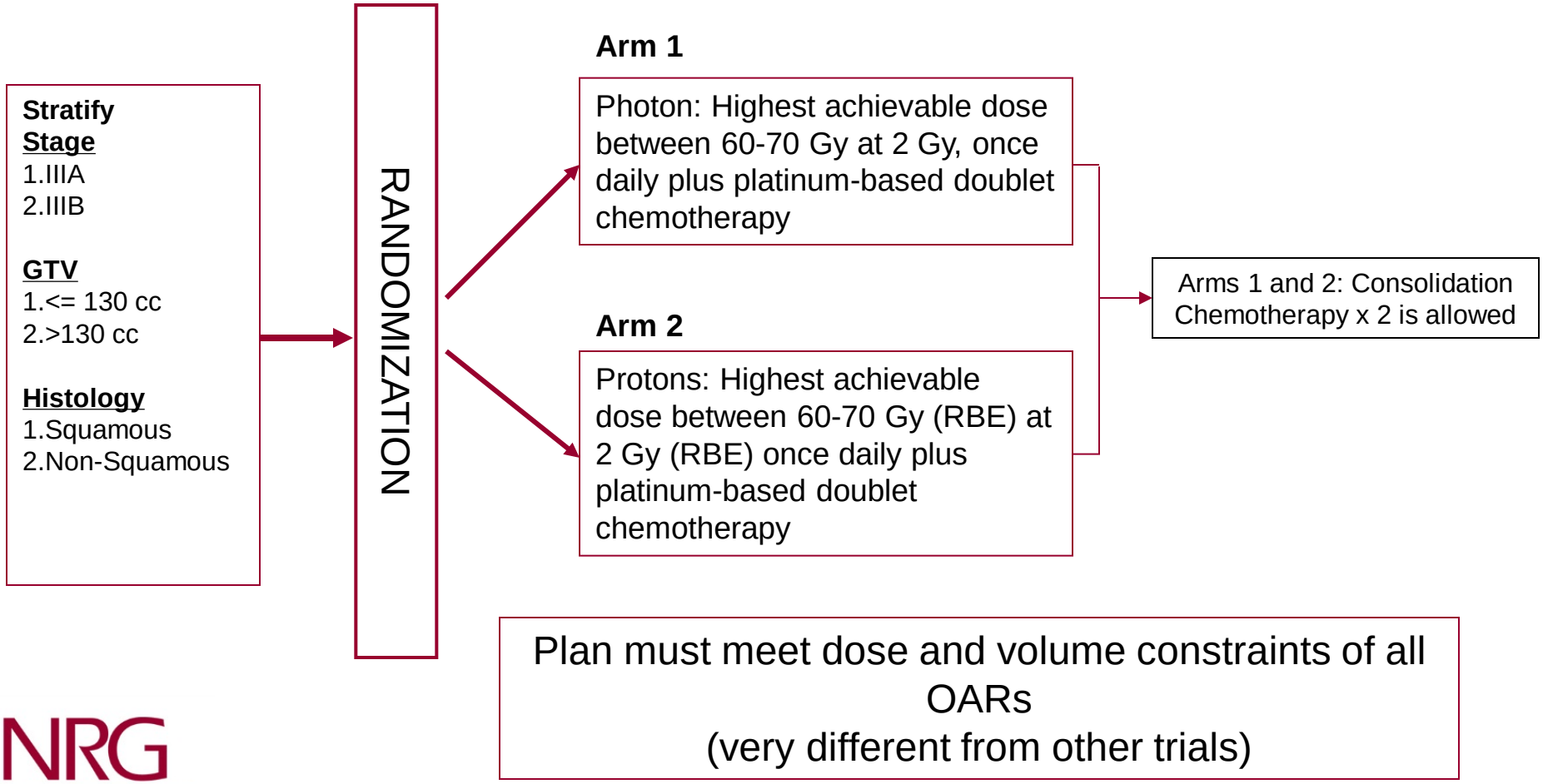
Initial PET/CT | **Mid-Tx PET/CT**



NRG/RTOG 1106
~3 wks

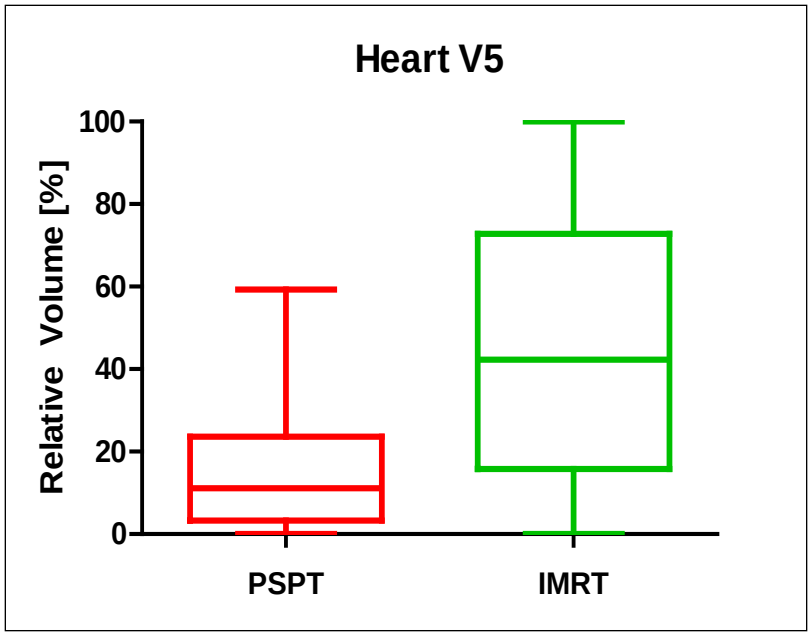
Proton Beamline

NRG/RTOG 1308: Phase III Randomized Trial Comparing Overall Survival after Photon vs Proton Chemo-RT for Stage II-IIIB NSCLC

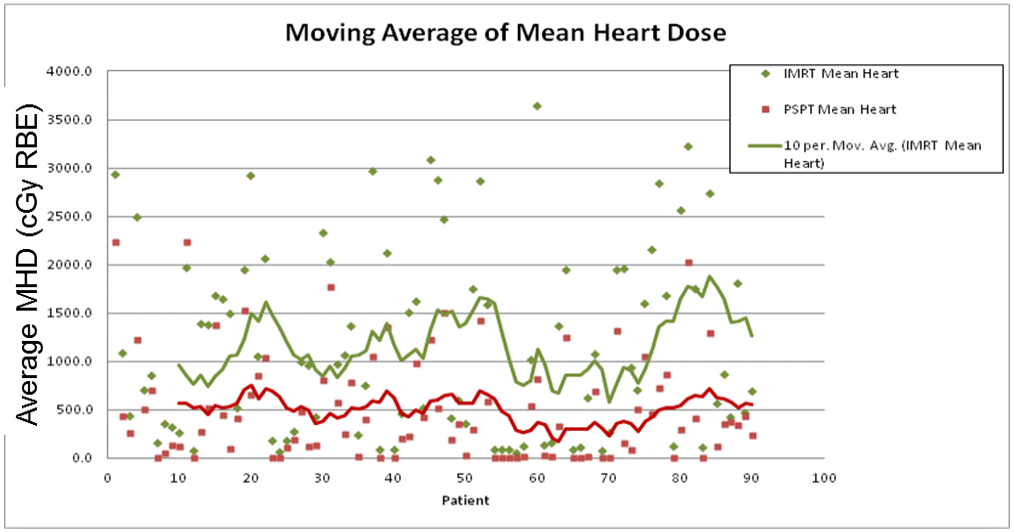


NRG ONCOLOGY™

Heart Dose: Protons vs IMRT



IMRT vs. PSPT - Latest Results



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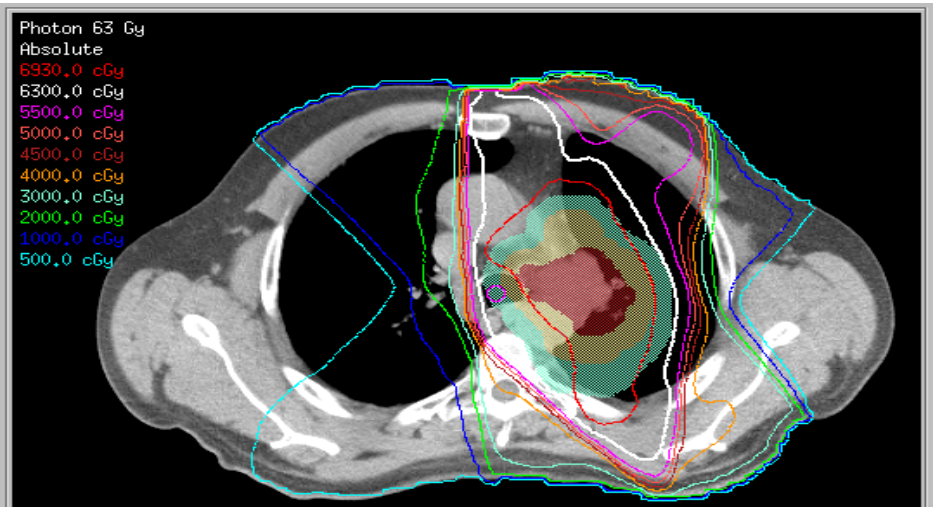
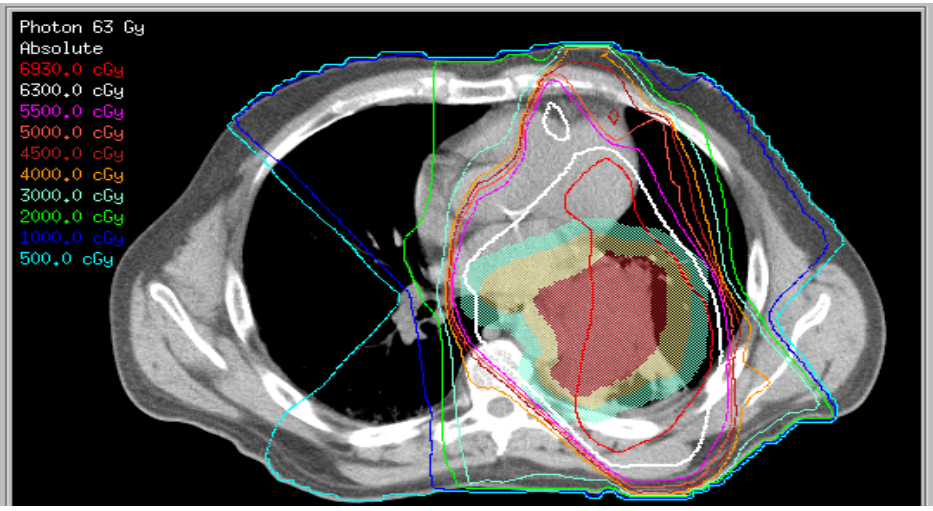
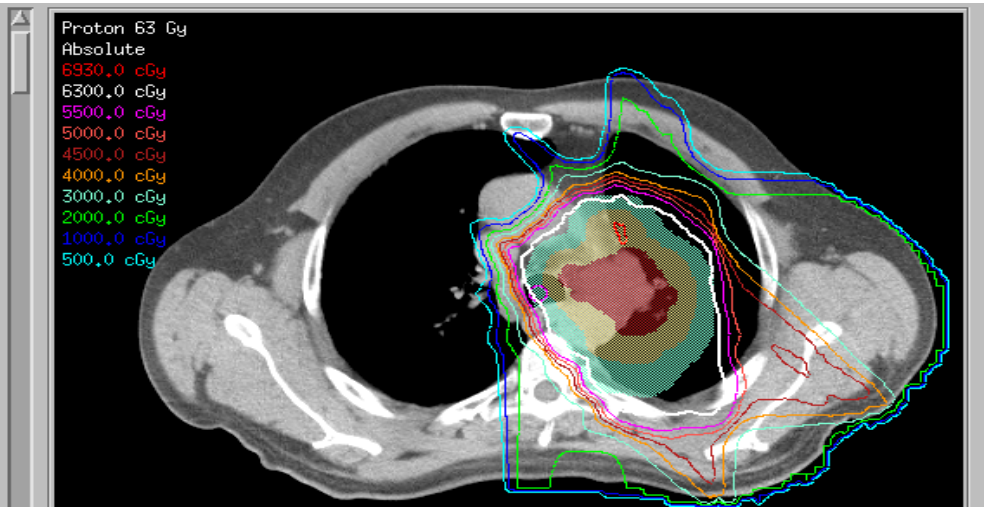
3D vs Proton for NSCLC

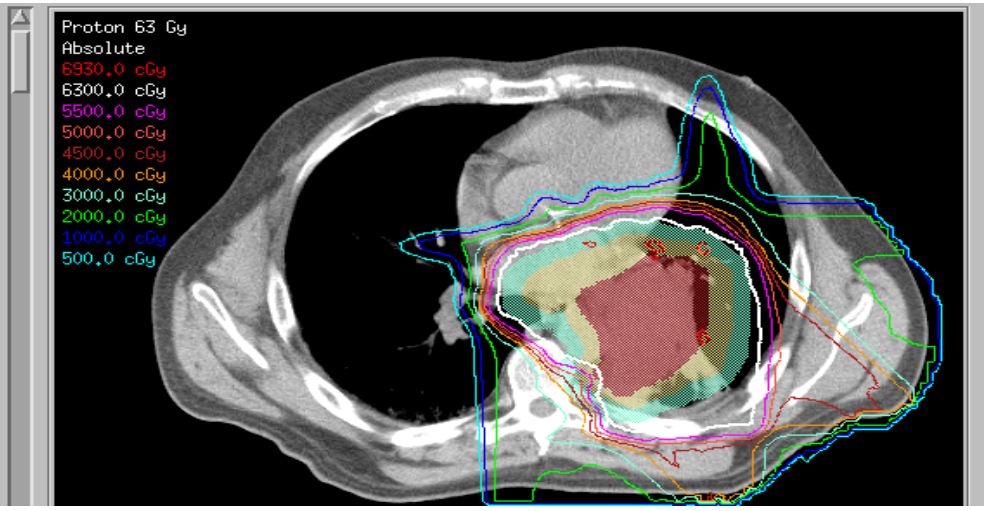
Photon 3D-CRT





Proton





Are Such Trial Strategies Possible for Other Tumor Types?

- Is there a Biologic +/or Biophysical Rationale?
- Are there Appropriate Targets +/or Targeting Agents?
- Does NCTN Have the Resources for Such Strategies?
- Candidate Disease Sites:
  - Melanoma
  - Malignant Brain Tumors
  - Selected Gastrointestinal Cancers

COG: Transforming the Outcome in Ph+ ALL

VOLUME 27 · NUMBER 31 · NOVEMBER 1 2009

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

From the Children's Oncology Group; Department of Pediatrics, Division of Hematology, Oncology, and Blood and Marrow Transplant, British Columbia's Children's Hospital, University of British Columbia, Vancouver, BC; Cook Children's Medical Center, Hematology and Oncology, Fort Worth; Pediatric Hematology and Oncology, University of Texas Southwestern Medical Center, Dallas, TX; Phyllis and David Komansky Center for Children's Health, Weill Cornell Medical Center, New York; Department of Pediatrics, New York University Medical Center, New York, NY; Department of Pediatrics and University of Florida Shands Cancer Center, University of Florida College of Medicine; Children's Oncology Group Statistics and Data Center, and the Department of Epidemiology and Health Policy Research, University of Florida, Gainesville, FL; Department of Preventive Medicine, University of Southern California; Hematology and Oncology Children's Hospital Los Angeles, Los Angeles; Children's Oncology Group Coordinating Center, Arcadia, CA; Pediatric Hematology and Oncology, The Children's Hospital and University of Colorado Cancer Center, Aurora, CO; Stem Cell Transplantation, Children's Hospital Medical Center Cincinnati, Cincinnati; Department of Pathology, The Ohio State University, Columbus, OH; Thomas Jefferson University, Philadelphia, PA; Department of Radiation Oncology, Nova Scotia Cancer Centre and Dalhousie University, Halifax, NS; Midwest Children's Cancer Center, Department of Pediatrics, Medical College of Wisconsin and Children's Hospital of Wisconsin, Milwaukee, WI; University of Alabama at Birmingham, Birmingham AL; and Department of Pathology, Johns Hopkins Hospital, Baltimore, MD.

Improved Early Event-Free Survival With Imatinib in Philadelphia Chromosome–Positive Acute Lymphoblastic Leukemia: A Children's Oncology Group Study

Kirk R. Schultz, W. Paul Bowman, Alexander Aledo, William B. Slayton, Harland Sather, Meenakshi Devidas, Chenguang Wang, Stella M. Davies, Paul S. Gaynon, Michael Trigg, Robert Rutledge, Laura Burden, Dean Jorstad, Andrew Carroll, Nyla A. Heerema, Naomi Winick, Michael J. Borowitz, Stephen P. Hunger, William L. Carroll, and Bruce Camitta

See accompanying editorial on page 5121 and articles on pages 5168 and 5189

A B S T R A C T

Purpose

Imatinib mesylate is a targeted agent that may be used against Philadelphia chromosome–positive (Ph+) acute lymphoblastic leukemia (ALL), one of the highest risk pediatric ALL groups.

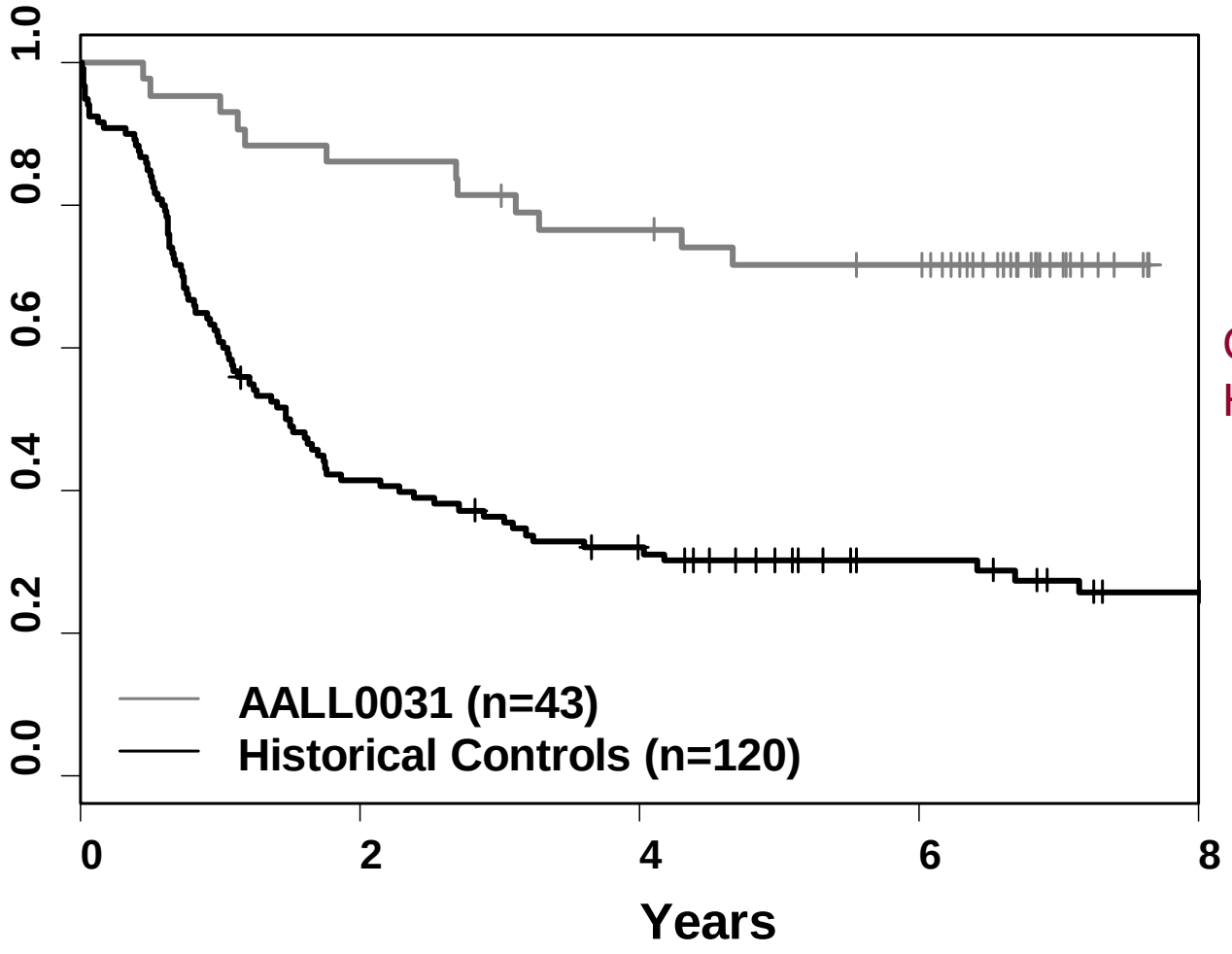
Patients and Methods

We evaluated whether imatinib (340 mg/m^2/d) with an intensive chemotherapy regimen improved outcome in children ages 1 to 21 years with Ph+ ALL (N = 92) and compared toxicities to Ph− ALL patients (N = 65) given the same chemotherapy without imatinib. Exposure to imatinib was increased progressively in five patient cohorts that received imatinib from 42 (cohort 1; n = 7) to 280 continuous days (cohort 5; n = 50) before maintenance therapy. Patients with human leukocyte antigen (HLA) –identical sibling donors underwent blood and marrow transplantation (BMT) with imatinib given for 6 months following BMT.

Results

Continuous imatinib exposure improved outcome in cohort 5 patients with a 3-year event-free survival (EFS) of 80% ± 11% (95% CI, 64% to 90%), more than twice historical controls (35% ± 4%; $P < .0001$). Three-year EFS was similar for patients in cohort 5 treated with chemotherapy plus imatinib (88% ± 11%; 95% CI, 66% to 96%) or sibling donor BMT (57% ± 22%; 95% CI, 30.4% to 76.1%). There were no significant toxicities associated with adding imatinib to intensive chemotherapy. The higher imatinib dosing in cohort 5 appears to improve survival by having an impact on the outcome of children with a higher burden of minimal residual disease af-

COG: Long-Term Results: Ph+ ALL



7 Year DFS

Chemo + Imatinib 72%

Historical control 27%

Schultz, JCO, 2009; updated Sept 2013

State of Georgia: NCTN Lost Opportunity?

- Historic Underperformer in Cooperative Group Trials
- 2014
  - New LAPS U10 (Winship Cancer Institute)
  - New Minority NCORP (GA Regents/Morehouse)
  - New Georgia CORE NCORP (Many Sites)
  - Savannah Site Participating in Another NCORP
  - 33+% Minority Enrollment at Most Georgia Sites
  - 8th Most Populous State

State of Georgia: Lost NCTN Opportunity?

- Tremendously Expanded Public Cancer Trials Network
- Insufficient Number of NCTN Trials
- Insufficient Number of Patient Slots in NCTN Trials
- All Noted Networks will Reach/Exceed Target Enrollment
- Significant Lost Opportunity?

NCTN Groups Summary

- Amazing Adaptation of Groups to New System!
- Trials in NCTN Limited by Available Resources
- Governance of NCTN Needs Definition
- What are Unintended Consequences of Transition?
- Great Need for Resources in Project Development